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Formulation and Evaluation of Self Nano Emulsifying Drug Delivery System Containing Mesalamine

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ABSTRACT

The Self-Nano Emulsifying Drug Delivery System (SNEDDS) represents a modern strategy to improving the oral availability of poorly water-soluble medication. The two main goals of the study were to design and evaluate mesalamine containing S-SNEDDS that would deliver the medicine particularly to the colon, increasing its oral bioavailability, and to investigate the characteristics of biosurfactants as pharmaceutical emulsifiers for L-SNEDDS. The optimal formulations were determined using a pseudo-ternary phase diagram comprising olive oil as the oil phase, biosurfactant as the surfactant, and PEG-400 as the co-surfactant. The solid adsorption process was employed to transform L-SNEDDS into free-flowing S-SNEDDS, using Syloid 244FP as the solid carrier. Out of 63 patients, 36 patients with small varices (F1/F2) and 27 with larger (F3) varices were detected on endoscope. Significant increase in mean splenic index from low (86.7 +/- 27.4) to high (94.7 +/- 27.7) grade varices was documented. Opposite trend was found with platelets (120.2 +/- 63.5 to 69.8 +/- 36.1) and platelets/ splenic diameter ratio (1676.7 to 824.6) declining significantly. Logistic regression showed splenic collaterals and platelets are significantly but negatively associated with esophageal varices grades. The evaluation of mesalamine-loaded L-SNEDDS revealed the following results: a transmittance of 85.57%, clear dispersibility, rapid self-emulsification within one minute, globule size of up to 100 nm, zeta potential of -31 mV, transmission electron microscopy (TEM) analysis, and an entrapment efficiency of 94.40%. Additionally, in vitro cell viability assays, micrometric characteristics, Fourier-transform infrared (FTIR) spectroscopy, drug content of 97%, and in vitro study of S-SNEDDS were also conducted. The findings indicate that biosurfactants serve as effective emulsifiers for L-SNEDDS, enhancing emulsifying property and stabilizing dispersions over time. Batch MF6 was optimized based on globule size, entrapment efficiency, and release profiles, demonstrating an improved dissolution rate compared to the marketed formulation.

Keywords: Mesalamine; SNEDDS; Ulcerative colitis; Biosurfactant; Bioavailability; FTIR; TEM; Entrapment Efficiency; Zeta Potential.

1. Introduction

Oral route remains the preferred route for delivering drugs due to its safety, ease of use for patients, and for self-administration. Absorption of drugs requires to be dissolved in the GI tract; otherwise, the drug may not be fully absorbed, have a low bioavailability, and cause a significant degree of variability when taken orally. Approximately one-third of the newly discovered therapeutic agents exhibit poor oral bioavailability due to a lack of sufficient water solubility [1]. Numerous lipids containing formulations have been examined in recent days to enhance oral bioavailability and clinical effectiveness [2]. Self-nanoemulsifying drug delivery systems (SNEDDS) are multi-component system that consists of a lipophilic drug combined with oil, a surfactant and a co-solvent. In recent years, these systems have gained significant interest for their ability to increase the bioavailability of poorly water-soluble drugs. These formulations spontaneously create a transparent nanoemulsion that allows the medicine to dissolve in gastrointestinal fluids when they come into touch with them and are impacted by motions and digestive processes in the gastrointestinal system [3]. Ulcerative colitis (UC) a chronic inflammatory disorder that mainly affects the inner lining of the colon. For treatment, mesalamine, also referred to as 5-aminosalicylic acid or 5-ASA, is regarded as the primary medication for addressing mild to moderate cases of UC [4]. Its mechanism involves inhibiting IL-1 and TNF-α. Furthermore, it also hinders the degranulation of mast cells, reduces the movement of neutrophils and macrophages, and inhibits the proliferation of T-cells [5]. Numerous investigations have focused on various formulations; however, there are still opportunities and challenges that must be addressed to enhance the market position of mesalamine. This is due to mesalamine's degradation in the gastrointestinal tract and its low rate of dissolution, which leads to inadequate bioavailability. The application of self-nanoemulsifying

drug delivery systems, or SNEDDS loaded with mesalamine addresses these issues, providing benefits such as improved bioavailability, decreased dosing frequency, sustained release effects, and targeted delivery to the colon through a pH-responsive method [6].

The frequent use of large amounts of chemically manufactured surfactants can result in drug degradation and instability, while also posing risks to the gastrointestinal system. In this study, to mitigate the harmful effects of surfactants We designed a mesalamine containing self-nano emulsifying drug delivery system that utilizes a Biosurfactant compound, which is a naturally derived substance that is both biocompatible and biodegradable [7]. Bacteria and yeast are examples of microorganisms that make biosurfactant compound. These biomolecules are recognized for their properties, including their capability to degrade substances, low toxicity levels, and functionality in extreme pH, salinity, and temperature conditions [8]. Numerous non-pathogenic yeast species produce huge quantities of Sophorolipids (SLPs), which are considered to be highly desirable glycolipid biosurfactants [9]. To lessen the potential toxicity associated with synthetic surfactants, the present research intended to design and assess mesalamine-loaded self-nanoemulsifying drug delivery systems (SNEDDS) using a biosurfactant as an emulsifying agent. Subsequently, the SNEDDS were evaluated for different dispersion characteristics, including Emulsification tests, droplet size, zeta potential, and thermodynamic stability.

1.1. Study Objectives

1) It is having ability to increase the bioavailability of poorly water-soluble drugs.
2) It would deliver the medicine particularly to the colon.
3) A transparent nanoemulsion that allows the medicine to dissolve in gastrointestinal fluids**.**
4) Mesalamine is regarded as the primary medication for addressing mild to moderate cases of ulcerative colitis.
5) Mesalamine containing self-nano emulsifying drug delivery system utilizes a biosurfactant compound, which is a naturally derived substance that is both biocompatible and biodegradable and doesn't cause drug degradation.

2. Material and Methods

2.1. Materials

PEG 400 from Research-Lab Fine Chem Industries, Mumbai, India; Biosurfactant from Siddhi Cosmo Pharma Dadar, Mumbai, India; Syloid® 244FP from Research-Lab Fine Chem Industries, Mumbai, India; and a generous gift sample of mesalamine were supplied by CTX Life Science Pvt. Ltd. in Gujarat, India.

2.2. Methodology

2.2.1. Preliminary selection of components

Studies on solubility and emulsification were used to choose the appropriate oil, surfactant, and cosurfactant. An excessive amount of the drug was incorporated into 2 ml of every excipient, and a Vortex mixer (Vortex mixer CM-10) was employed to aid in the dissolution process. Next, the vials were sealed and subjected to stirring in an ultrasonicator for 10 minutes to ensure thorough mixing of the drug and excipient. Subsequently, the mixtures were allowed to stabilize at 30°C for duration of 72 hours [10]. Prior to and following dilution, the equilibrated samples

were visually assessed and centrifuged for 10 min at 3500 rpm. After the combinations were diluted (1:100) for solubility, a UV spectrophotometer (Shimadzu) was used to analyze the % transmittance [11].

2.2.2. Pseudo-ternary phase diagram construction using the aqueous titration method

To ascertain the component concentration within the SNEDDS range, a pseudo ternary phase diagram was plotted at room temperature using a water titration method. The study involved oil (Olive oil), surfactant (Biosurfactant), and cosurfactant (PEG 400), combined in various ratios. The surfactant and cosurfactant, referred to as S_{mix}, were combined. In weight ratios of 2:1, 1:1, and 3:1, focus on varying the concentration of surfactant relative to cosurfactant. Each phase diagram required thorough mixing of oil and a appropriate Smix ratio in weight ratios of 1:9, 1:7, 1:5, 1:4, 1:3, 1:2, 1:1, To find the concentration of the components to precisely characterize phase boundaries, the concentration of each component should be measured in separate glass test tubes at a 2:1 ratio. 5% of the total volume was gradually added to the aqueous phase to reach concentrations between 5% and 95%. After two minutes of vertexing, the mixtures were left to equilibrate. following each addition. Oil, Smix, and water were represented on each axis of the ternary phase diagram, which was used to visually record and track changes in physical conditions that change from clear to cloudy and vice versa. The phase diagrams were plotted using CHEMIX school 12.5 software [12].

2.2.3. Formulation of L-SNEDDS

The formulation of Mesalamine containing SNEDDS was driven by reaching the highest solubility of mesalamine within a suitable oil phase, surfactant, and co-surfactant, such as Olive oil, Biosurfactant, and PEG 400 respectively. A predetermined amount of API was first dissolved in olive oil, and then equal volumes of a biosurfactant and PEG 400 mixture (Smix) were added [13]. This blend was mixed thoroughly until it formed a uniform liquid phase, after which eudragit®S-100 was incorporated into the above mixture. The mixtures underwent bath sonication for ten minutes to ensure even dispersion. The final formulation appeared clear with a slight yellow tint. The most stable formulation was selected for further investigation [14].

Table 1. Formulation table for mesalamine loaded L-SNEDDS

Batch No.	Mesalamine (mg)	Eudragit®S-100 (mg)	Olive oil (% V/V)	Biosurfactant: PEG400 (Smix % V/V)	Observations after a 24-hour period
F1	100	100	5	40	Phase separation
F2	100	100	5	60	Phase separation
F3	100	100	5	80	Stable and clear
F4	100	100	10	40	Phase separation
F5	100	100	10	60	Phase separation
F6	100	100	10	80	Stable and clear
F7	100	100	15	40	Phase separation
F8	100	100	15	60	Phase separation
F9	100	100	15	80	Phase separation

2.2.4. Solidification of L-SNEDDS

The process of solidification involved the surface adsorption technique. Onto a solid carrier, Syloid® 244FP, the optimized L-SNEDDS was absorbed and solidified. Gradually combining the L-SNEDDS formulation resulted in a moist mixture. This wet mass was then sieved through no.120 mesh to achieve free-flowing S-SNEDDS [15].

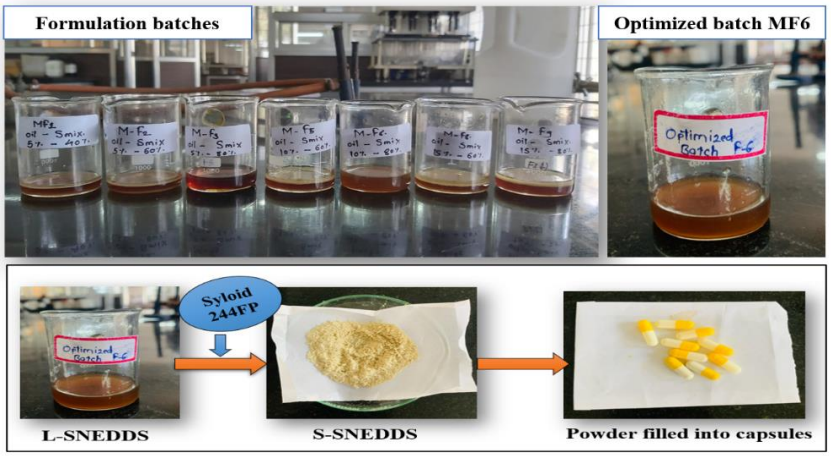

Figure 1. Transformation from L-SNEDDS to S-SNEDDS

3. Characterization of SNEDDS

3.1. % Transmittance

In order to determine the percentage of light transmission at 308 nm, ten times, 1 mL of distilled water was added to each composition. A UV spectrophotometer was then utilized for the measurement, with distilled water as the reference point [16].

3.2. Self-Emulsification and Dispersibility Assessment

Self-emulsification's efficacy and spreadability were evaluated with the USP dissolving apparatus 2. (ELECTROLAB dissolution tester). Each formulation, in a volume of 1 mL, was gradually added into 200 mL of 0.1 N HCl and PBS 6.8 solutions, kept at a constant temperature of 37°C. The mixtures were gently stirred with stainless steel paddles rotating at a speed of 100 rpm. Observations were made on the formulations to evaluate their emulsification efficacy, spreadability, physical stability, and overall appearance, after which they were rated according to a standardized grading system [17].

Grade A indicates that a bluish-looking nanoemulsion formed quickly (within one minute), Grade B indicates that a bluish-white nanoemulsion formed quickly (within two minutes), Grade C indicates that a milky nanoemulsion formed within two minutes, and Grade D indicates that a greyish-white, slightly oily nanoemulsion formed slowly (within more than two minutes). Large oil globules on its surface, designated Grade E, formed very slowly (more than three minutes), suggesting inadequate or poor emulsification [18].

3.3. Robustness Test

The chosen SNEDDS were diluted 100 times each with distilled water, 0.1 N hydrochloric acid, and a pH 6.8 phosphate buffer in order to assess their stability. At 37°C, these combinations were then agitated until they were

homogeneous. Following a full day at room temperature, they were examined visually to look for signs of phase separation [19].

3.4. Thermodynamic Stability Test

Investigations of thermodynamic stability were carried out on a few chosen formulations which includes,

A. Centrifugation Method: The formulations went through centrifugation at 3500 rpm. for a duration of 30 minutes. Phase separation, creaming, and cracking were among the instabilities seen throughout this process. Only the formulations that remained stable were selected for subsequent testing.

B. Heating cooling cycle Method: The samples were subjected to three phases of temperature changes, alternating between 45°C and 4°C in the refrigerator. At least 48 hours were spent maintaining each temperature. SNEDDS showed instabilities at the conclusion of each cycle. Formulations that passed these tests were put through a freeze-thaw cycle.

C. Freeze thaw cycle Method: The samples were subjected for three cycles of freezing and thawing, temperature ranging from -21°C to +25°C, maintaining every temperature for at least 48 hours. The stability of SNEDDS was assessed at the end of each cycle [20].

3.5. Analysis of zeta potential and Globules size

The formulations were diluted 1:1000 (v/v) in double-distilled water, and their globule size and zeta potential were measured. The chosen SNEDDS formulation's droplet size distribution was investigated using a particle size analyser [21].

3.6. Surface Morphology

The sample's morphological features were examined using electron microscopy via transmission (TEM), with preparation involving phosphotungstic acid staining [22].

3.7. Measurement of cloud points

The optimized formulation was diluted using deionized water in a 1:100 ratio and then heated gradually in a water bath. The temperature at which the solution turns cloudy that noted as the cloud point [23].

3.8. Drug Entrapment efficiency

The formulation of mesalamine-containing SNEDDS required the use of 20 mL of a suitable solvent. From this dispersion, a 1 ml sample was extracted, diluted further with the same sample, and centrifuged at 10,000× g. After being meticulously removed. A 0.45 µm membrane was used to filter the supernatant layer and examined using a UV spectrophotometer set to 302 nm. The entrapment efficiency has been estimated using the provided formula [24].

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Amount of drug in formulation}}{\text{Amount of drug added}} \times 100$$

3.9. In Vitro Drug release investigation of L-SNEDDS

A modified dialysis technique was used in the study to investigate the release of mesalamine from L-SNEDDS dispersion. Initially, for a whole day at room temperature, dialysis tubing has a molecular weight cutoff of 12,000–14,000 was immersed in a newly made release medium. A tubular cellulose dialysis bag was filled with a 1 ml portion of the freshly made L-SNEDDS formulation, which contained 10 mg of mesalamine equivalent. The formulation was diluted ten times with the release medium. These bags' ends were tightly sealed to avoid leaks, and they were then put in a shaking water bath with 100 rpm and 37°C, filled with 100 mL of release medium. 1 mL samples were collected at predetermined intervals, and new solution was added to the medium. These samples underwent filtration, were further diluted with the release medium, and then subjected to UV spectroscopic analysis [25].

3.10. In vitro cell viability assay

The National Centre for Cell Sciences in Pune provided the Colo 205 human colon cell line, which was cultivated in DMEM media administered 10% fetal bovine serum as a supplement. The cells were initially incubated at a density of 1 × 10^4 cells/ml in the culture medium for 24 hours at 37°C with 5% CO2. Subsequently, the cells were planted in 70µl of culture media, 100µl of sample (varying from 10 to 100 µg/ml), and 70¼l of cells per well in tissue culture-grade microplates with 96 wells. The cell line was placed in control wells with DMSO (0.2% in PBS). For accuracy, every experiment was carried out three times. Cell survival and the proportion of living cells after culture were evaluated using controls. In a CO2 incubator (Thermo Scientific BB150), the cell cultures were incubated once more for twenty-four hours at 37°C and 5% CO2. Following this time, 20 µl of MTT reagent (5 mg/ml in PBS) was added after the medium had been fully withdrawn. After adding MTT, the cells were cultured in the CO2 incubator for four more hours at 37°C. Under a microscope, the growth of formazan crystals showed that live cells had converted the yellow MTT to a dark-colored formazan. Following a thorough removal of the medium, 200µl of DMSO was added, and the samples were then incubated at 37°C. An Elisa microplate reader (Benesphera E21) set to 570 nm was used to measure the absorbance of each duplicate sample [26].

3.11. Micrometric characteristics of S-SNEDDS

To evaluate the micrometric characteristics of S-SNEDDS, we examined factors such as the angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio [27].

3.12. FTIR Examination

The IRAffinity-1S FTIR instrument was used to detect pure API and assess potential interactions between medication compounds, oils, surfactants, and cosurfactants utilizing infrared absorption [28].

3.13. In vitro dissolution investigations of S-SNEDDS

To explore the impact of a SNEDDS on drug release, Using USP type I dissolution device (ELECTROLAB dissolution tester) with 900 ml of simulated intestinal and stomach fluids dissolution tests were carried out. Initially, 0.1 N HCl, which is an acidic solution, was applied for the first three hours. This was succeeded by PBS at a pH of 7.4, simulating intestinal conditions, for a duration of four to six hours. Subsequently, PBS at a pH of 6.8,

representing colonic conditions, was utilized for the following six to twelve hours. A continuous speed of 50 ± 5 rpm and a temperature of 37 ± 0.5°C were maintained for the apparatus. 1.0 mL aliquots of the samples were removed and replaced with new dissolving medium after the samples were collected at predetermined intervals of 0, 0.5, 1, 2, 3, 4, 6, and 8 hours. The gathered samples were suitably diluted with the mobile phase, and a Shimadzu UV spectrophotometer was used to measure the drug content at 302 nm for 0.1 N HCl and 331 nm for PBS-7.4 and PBS-6.8 [29].

3.14. Accelerated Stability Investigation

According to the ICH criteria that apply to Zone III, the meticulously honed formulation was kept in a container for three months at a temperature of 40 degrees Celsius, plus or minus two degrees, and a relative humidity of 75%, ± 5% [30].

4. Result and Discussion

4.1. Result

4.1.1. Preliminary selection of components

Screening of suitable oil, surfactant and cosurfactant was carried out on the basis of solubility and emulsification studies. The solubility of mesalamine was examined through experiments involving various oils, co-surfactants, and surfactants, excess amount of drug is added into the 2 ml of each excipient. A vortex mixer (Vortex mixer CM-10) was used to facilitate the solubilization. Mesalamine was shown to dissolve best in PEG-400, olive oil, and a bioactive surfactant. As a result, these compounds were selected as the co-surfactant, surfactant, and oil phase, respectively as illustrated in Figure no.2 and table no.2.

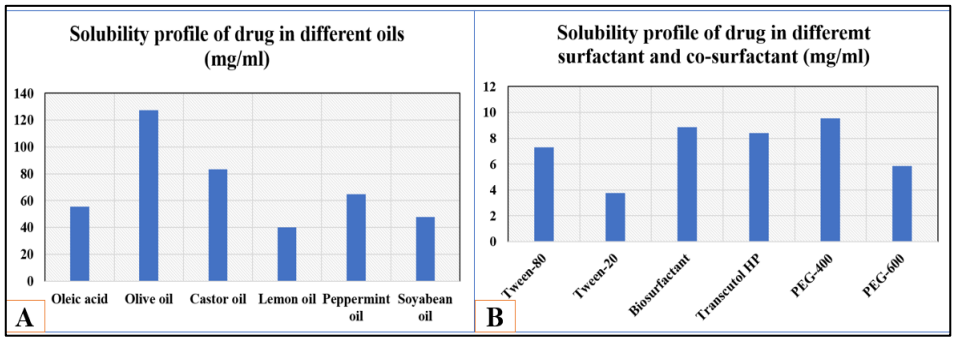

Figure 2. Solubility profile of drug in different oils, surfactant and co-surfactant (mg/g)

Table 2. Solubility results of mesalamine in various oils, surfactants and co-surfactants (mean ± SD; n=3)

Oils	Solubility (mg/g)	Surfactants and Co-surfactants	Solubility (mg/g)
Oleic acid	55.64±4.19	Tween-80	7.31±0.57
Olive oil	127.32±8.50	Tween-20	3.75±0.88
Castor oil	83.38±4.04	Biosurfactant	8.86±0.32
Lemon oil	40.16±3.38	Transcutol HP	8.41±1.38
Peppermint oil	64.65±2.52	PEG-400	9.54±1.78
Soyabean oil	47.65±2.52	PEG-600	5.87±0.45

4.1.2. Pseudo ternary phase diagram construction using the aqueous titration method

In order to determine the concentration of components for the existing range of the SNEDDS, a pseudo ternary phase diagram was constructed at ambient temperature using a water titration method. Oil (Olive oil), surfactant (Biosurfactant) and cosurfactant (PEG 400) were grouped in different combinations for phase studies. The study used Biosurfactant/PEG400 (Smix) mixed with olive oil in different ratios (A-mix at 1:1, B-mix at 2:1, and C-mix at 3:1 as described in Figure No. 3) to generate pseudo-ternary phase diagrams. The ternary plot was created using the particular concentrations that showed the maximum nano emulsification region.

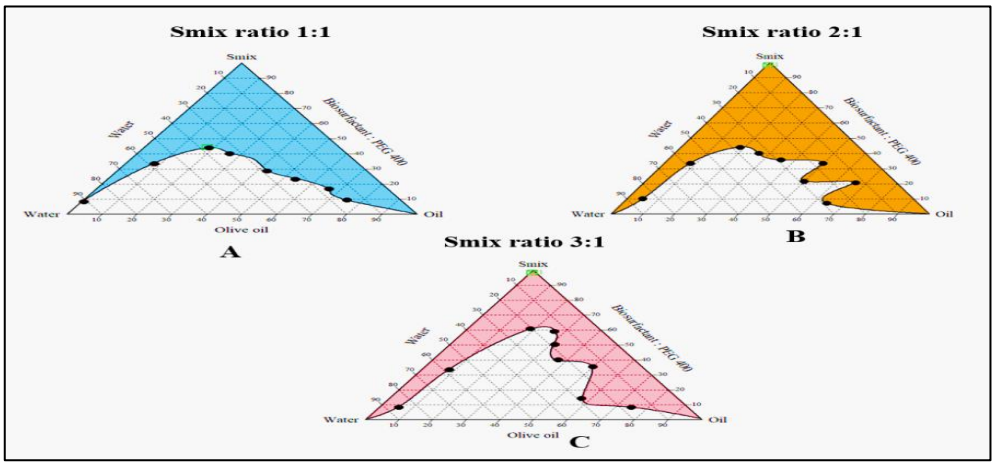

Figure 3. Ternary plot of different S_{mix} ratios (1:1, 2:1, 3:1)

4.1.3. % Transmittance

The percentage of light transmitted through the SNEDDS provided insights into formulation characteristics such as droplet size and uniformity. Using the % Transmittance test, each formulation batch was assessed; batch F3 and batch F6 had the highest % Transmittance, surpassing 95%.

4.1.4. Self-Emulsification and Dispersibility Assessment

The efficiency and dispersibility of self-emulsification were determined through USP dissolution apparatus type II (ELECTROLAB dissolution tester) According to the results, both F3 and F6 passed the dispersibility test with a Grade A, as described in table no.3.

Table 3. Self-Emulsification and Dispersibility Assessment

Formulation Batch	Emulsification Time	Appearance	Grade
F3	Less than one minute	Clear	A
F6	Less than one minute	Clear	A

4.1.5. Thermodynamic stability

The Stability of the prepared L-SNEDDS formulations at various stress conditions was evaluated by heating cooling cycles (4°C and 40°C) and freeze thaw cycles (-21°C and +25 °C) with storage at specified temperature for 48h. According to the results, the selected formulation passed the test with the exception of F3, which failed to sufficiently preserve SNEDDS stability during the Freeze Thaw cycle, as illustrated in Table No. 4.

Table 4. Thermodynamic stability of SNEDDS

Stability Test	F3	F6
Centrifugation Test	Yes	Yes
Heating Cooling cycle	Yes	Yes
Freeze Thaw cycle	No	Yes

4.1.6. Robustness to dilution

The robustness of selected SNEDDS by diluting them with distilled water, 0.1 N HCl, and pH 6.8 phosphate buffer (diluted 100 times). Nano-emulsions After a day, there were no indications of separation or drug precipitation. in a variety of dilutions, including pure water, 0.1 N HCl, and PBS-6.8.

4.1.7. Globule size and zeta potential analysis

Size characterization is one of the most essential examinations for SNEDDSs development since the size of the particles can directly affect not only the in vitro tested characteristics.

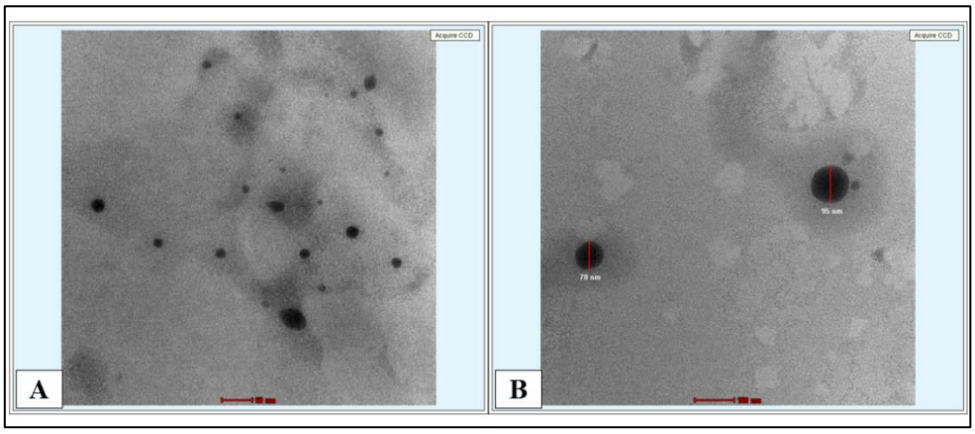

Figure 4. TEM images of optimized batch MF6

4.1.8. Measurement of cloud point

The cloud point is known as the temperature at which the nano/emulsion is broken. The cloud point is determined to investigate the stability of SNEDDSs in the GI tract. The cloud point of SNEDDS should be more than 37 C; otherwise, absorption of the drug can be interrupted, the cloud point of the optimized batch was 65°C±1°C, which represents that the resulting nano emulsion is stable in vivo.

4.1.9. Entrapment efficiency and drug content determination

With an entrapment efficiency of 94.40% and a drug content of 97.26%, the mesalamine containing SNEDDS showed very positive results.

4.1.10. In vitro dissolution investigations

Assessment of drug release from formulations is essential as it indicates the possible gastric dissolution and could be a probable tool to forecast the absorption of low aqueous soluble drugs. Therefore, the in vitro release test was conducted for the mesalamine capsule loaded with SNEDDS and compared with the S-SNEDDS and marketed

tablet. Figure 6 shows the results of the in vitro dissolving tests for L-SNEDDS, S-SNEDDS, and a commercial tablet. In contrast to the marketed tablet's 65.64% drug release rate, L-SNEDDS and S-SNEDDS exhibit substantially higher rates, at 96.82% and 95.76%, respectively, according to the drug release statistics. The SNEDDS formulation has shown a notable improvement in entire drug release.

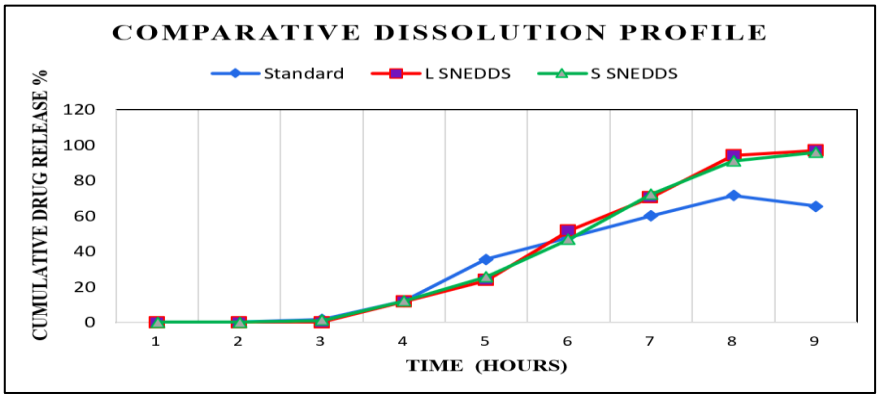

Figure 5. Comparative dissolution profile of L-SNEDDS, S-SNEDDS and Standard

4.1.11. Accelerated Stability Investigation

No notable alterations were noticed following three months of storage at accelerated temperatures of 40±2 °C and 75±5% relative humidity.

4.1.12. In vitro cell viability assay

The in vitro cell viability assay was carried out using MTT assay. This Colorimetric assay is based on the capacity of Mitochondria succinate dehydrogenase enzymes in living cells to reduce the yellow water-soluble substrate 3-(4, 5-dimethyl thiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) into an insoluble, purple colored formazan product which is measured spectrophotometrically. Since reduction of MTT can only occur in metabolically active cells, the level of activity is a measure of the viability of the cells.

Table 5. MES SNEDDS-6's effects on the colon cell line COLO 205 using the MTT assay

S.No.	Concentration (µL)	Absorbance (OD)				% Cell viability	% Inhibition
		1	2	3	Average		
1	Control	1.568	1.624	1.587	1.593		
2	10	0.867	0.815	0.835	0.839	52.66792	47.33208
3	20	0.711	0.731	0.716	0.716	44.94664	55.05336
4	40	0.687	0.614	0.621	0.640667	40.21762	59.78238
5	80	0.548	0.523	0.537	0.536	33.64721	66.35279
6	100	0.512	0.501	0.522	0.511667	32.11969	67.88031

4.2. Discussion

To develop a dosage form that is stable, safe, and effective, Preformulation studies are conducted. Mesalamine undergone Preformulation studies, which included organoleptic experiments examining appearance, color, odour, and taste. Screening of suitable oil, surfactant and cosurfactant was carried out on the basis of solubility and

emulsification studies. Mesalamine showed highest solubility in olive oil (127.32±8.50 mg/g) as compared to other oils so olive oil was selected as oil phase. Solubility of mesalamine was examined in all surfactants and co-surfactants. Mesalamine showed higher solubility in biosurfactant (sophorolipid glycolipid which is 8.86±0.32 mg/g) than Tween-80 and in propylene glycol-400 co- surfactants (9.54±1.78).

Based on the results of solubility studies, ternary phase diagram of the Olive oil (oil), Biosurfactant (surfactant) and PEG-400 (co-surfactant) was constructed to evaluate the self- emulsifying properties of the compositions and to determine the concentration range of components for formation of a clear nano emulsion. The pseudo-ternary phase diagrams consisted of Biosurfactant/PEG400 (Smix) with ratio 1:1 showed maximum nano-emulsification region hence this ratio (1:1) was selected to make formulation. All formulation batches were assessed with % Transmittance test, out of them batch F3 and F6 showed highest % Transmittance, 97± 0.06 % and 98± 0.00 % respectively. For self-emulsification and dispersibility assessment result showed that F3, F6 showed Grade A in dispersibility test, with emulsification time about 35-46 Seconds.

From thermodynamic stability test, was known that selected formulation passed the test except for F3 was not sufficient to ensure the stability of SNEDDS during Freeze Thaw cycle. The droplet size of the optimized SNEDDS was found to be between 50.5±3.17 to 100.35±3.5 nm, and the polydispersity index was found to be between 0.578±0.05and 0.756±0.01. The zeta potential was observed to be -31mV. An in vitro release study was conducted for L-SNEDDS, S-SNEDDS which is then compared with marketed tablet of mesalamine in different dissolution medium. The comparative dissolution profiles of L-SNEDDS, S-SNEDDS and marketed tablet are shown in Figure No. 6. SNEDDS formulation exhibited enhancement in cumulative drug release. Mesalamine containing SNEDDS formulations were examined under In vitro cell viability assay. According to the results shown in Table 3, the colo-205 cell line exhibits a significant dose-dependent inhibition that ranges from 10 to 100 µL. Thus, against the colo-205 cell line, mesalamine containing SNEDDS exhibit anti-ulcer capabilities.

5. Conclusion

In our research, we explored the use of Bio-surfactants as effective emulsifiers for L-SNEDDS, which enhance emulsifying property and make dispersion stable over extended periods. Our research indicates that using olive oil as the oil phase, biosurfactant as the emulsifier, and PEG-400 as a co-surfactant in a 10:40:40% v/v ratio yields the optimal SNEDDS preconcentrate for improving mesalamine solubility. The MF6 batch was optimized based on globule size, entrapment efficiency, and release pattern, demonstrating a superior dissolution rate compared to commercial formulations. Mesalamine containing SNEDDS exhibit anti-ulcer properties against the colo-205 cell line. Given the current scenario, the frequent consumption of poor diets by people has led to numerous gastrointestinal issues, posing a global health challenge. A self-nano emulsifying drug delivery system might offer a more effective solution with enhanced bioavailability for treating these conditions.

Declarations

Source of Funding

This study did not receive any grant from funding agencies in the public, commercial, or not–for–profit sectors.

Competing Interests Statement

Both the contributing authors declare no conflicts of interest.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

Both the authors took part in literature review, analysis, and manuscript writing equally.

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